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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/753,143	01/02/2001	Nathan Ellis	63475/263	1780

7590 04/22/2003

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EXAMINER	
KERR, KATHLEEN M	

ART UNIT	PAPER NUMBER
1652	9

DATE MAILED: 04/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/753,143	ELLIS ET AL.	
	Examiner	Art Unit	
	Kathleen M Kerr	1652	

-- *The MAILING DATE of this communication appears on the cover sh et with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 October 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 October 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Application Status

1. By virtue of a preliminary amendment filed on October 5, 2001 (Paper No. 6), Claims 1-10 and 21-85 have been cancelled. Claims 11-20 are pending in the instant Office action and will be examined herein.

Priority

2. The instant application is granted the benefit of priority for the U.S. non-Provisional Application No. 09/175,828 and 08/559,303 filed on October 20, 1998 and November 15, 1995, respectively, as requested in the first lines of the specification.

Information Disclosure Statement

3. No information disclosure statement has been filed with the instant application as of the date mailed of the instant Office action. Applicants are reminded that they have a duty to disclose all information, of which they are aware, relevant to the patentability of the pending claims (see 37 C.F.R. § 1.56 and M.P.E.P. § 2000) and that the parent application each contain a list of cited references.

Compliance with the Sequence Rules

4. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to **fully** comply with the requirements of 37 C.F.R. § 1.821

through 1.825; Applicants' attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990).

a) In Figure 2, DNA and protein sequences are disclosed without benefit of SEQ ID NOs.
b) In Figure 3, a DNA sequence is disclosed without benefit of a SEQ ID NO.
c) In Figure 4, four protein sequences are disclosed without benefit of SEQ ID NOs.
d) On page 14, lines 25-26, two oligonucleotides are disclosed without benefit of SEQ ID NOs.
e) On page 15, line 9, two oligonucleotides are disclosed without benefit of SEQ ID NOs.
f) On page 16, line 26, an oligonucleotide is disclosed without benefit of a SEQ ID NO.
g) On page 17, line 6, an oligonucleotide is disclosed without benefit of a SEQ ID NO.
h) On page 17, line 8, an oligonucleotide is disclosed without benefit of a SEQ ID NO.
i) On page 17, line 34, two oligonucleotides are disclosed without benefit of SEQ ID NOs.
j) On page 36, in Table 2, numerous DNA sequences are disclosed without benefit of SEQ ID NOs.

If the noted sequences are in the sequence listing as filed, Applicants must amend the specification to identify the sequences appropriately by SEQ ID NO. If the noted sequences are not in the sequence listing as filed, Applicants must provide (1) a substitute copy of the sequence listing in both computer readable form (CRF) and paper copy, (2) an amendment directing its entry into the specification, (3) a statement that the content of the paper and CRF copies are the same and, where applicable, include no new matter as required by 37 C.F.R. § 1.821 (e) or 1.821(f) or 1.821(g) or 1.821(b) or 1.825(d), and (4) any amendment to the specification to identify the sequences appropriately by SEQ ID NO.

Objections to the Specification

5. The specification is objected to for being confusing with respect to the sequence listing. The sequence listing contains 78 sequences filed on October 5, 2001. Each of the 78 SEQ ID NOs is not mentioned in the specification and/or the claims. It is unclear why said sequences are in the sequence listing if they are not described in the specification. All SEQ ID NOs in the sequence listing must be described in the specification. Appropriate correction is required.

6. In the specification, the Abstract is objected to for not completely describing the disclosed subject matter (see M.P.E.P. § 608.01(b)). It is noted that in many databases and in foreign countries, the Abstract is crucial in defining the disclosed subject matter, thus, its completeness is essential. The Examiner suggests the inclusion of the definition of the abbreviation "BS" and the inclusion of a reference to human samples for completeness.

7. The specification is objected to for lacking appropriate continuity data in the first paragraph. The instant application claims the benefit of U.S. non-Provisional Application No. 08/559,303 and 09/175,828 as continuations; however, different subject matter is being claimed in the instant application with respect to the parent applications rendering the instant application a ---divisional--- of the parent applications. Appropriate amendment to the specification is required (see M.P.E.P. § 201.11).

8. The specification is objected to for having improper citations of references as follows:

a) On page 3, line 33, the Straughen citation is incomplete.
b) On page 5, line 4, the Ellis citation is incomplete.
c) On page 13, line 29, the German citation is incomplete.
d) On page 26, line 26, the Ellis citation is incomplete.

Appropriate correction is required.

Claim Objections

9. Claim 13 is objected to under 37 C.F.R. § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the

claim(s) in independent form. The term "mutated BLM gene" is defined on page 8 of the instant specification as being the normal form with one or more deletions, insertions, point mutations, or rearrangement mutations. Thus, these limitations in Claim 13 cannot further limit the scope of Claim 11.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 11-20 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "*BLM* gene" us unclear. Said term is described in the specification as being linked to Bloom's syndrome. A particular gene described in the specification is further described on page 29 as a putative DNA helicase. It is unclear if the term in the claim means a mutant of the putative DNA helicase or if the term means any gene linked to Bloom's syndrome. Clarification is required.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 11-20 are rejected under 35 U.S.C. § 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 11 is drawn to methods of determining if a subject carriers a mutated BLM gene; the instant rejection is set forth based on a broad interpretation of the term "BLM gene" wherein its definition encompasses *any* gene linked to Bloom's syndrome.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." University of California v. Eli Lilly and Co., 1997 U.S. App. LEXIS 18221, at *23, quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these.

In the instant specification, a single example of a Bloom's syndrome-linked gene is described. The structure of this gene is adequately described. However, no description of the genus of all Bloom's syndrome-linked genes is described. No common structure and/or function is offered so that one of skill in the art would be able to predict the structure or function (other than its disease identification) of other Bloom's syndrome-linked genes. This genus of structure

must be described in order to adequately describe the genus of claimed methods. Thus, the instant claims are not adequately described by the specification.

12. Claims 11-20 are rejected under 35 U.S.C. § 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 11 is drawn to methods of determining if a subject carriers a mutated BLM gene; the instant rejection is set forth based on an interpretation of the term "BLM gene" wherein its definition encompasses a gene related specifically to the disclosed BLM gene.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." University of California v. Eli Lilly and Co., 1997 U.S. App. LEXIS 18221, at *23, quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these.

In the instant specification, a mutated BLM gene is described as SEQ ID NO:72 with any number of deletions, insertions, point mutations, and/or rearrangements mutations (see page 8). Thus unlimited mutation broadens the scope of a "mutated BLM gene" to be virtually *any* structure. In the instant specification, a single example of a human Bloom's syndrome-linked gene is described. However, in view of this broad interpretation of a "mutated BLM gene" defined in the specification, no common structure of the genus of mutated BLM genes can be recognized. Moreover, the instant claims are drawn to identifying mutated BLM genes from other species while none are described. Thus, the instant claims are not adequately described by the specification.

The Examiner suggests adding method steps to the instant claims that utilize SEQ ID NO:72 in some hybridization step. Such claims would limit the scope of a "mutated BLM gene" by virtue of the hybridization language.

13. Claims 11-20 are rejected under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for methods for determining mutated BLM genes that are closely related to the BLM gene disclosed, does not reasonably provide enablement for methods for determining mutated BLM genes that are not related to the disclosed gene. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. The instant claims are drawn to methods of determining the presence of a mutated BLM gene wherein the definition of mutated BLM gene is so broad that numerous species of the genus would not be recognized by common techniques in the art. As such, these structurally dissimilar,

mutated BLM genes would require undue experimentation for their detection. To identify such genes would require undue experimentation.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

The specification describes examples of using the disclosed BLM gene to identify BLM genes in other subjects. The subject's BLM gene can then be compared to the wild type, or normal, BLM gene. No working examples are described wherein the mutated BLM gene is significantly different in structure from the disclosed BLM gene. No guidance for surmounting such problems is offered. While the relative skill of those in the prior art is high, the

predictability of identifying mutated BLM genes is strictly linked to the ability to find the mutant gene by its structural relationship to that which is disclosed in the instant specification. The predictability of finding highly dissimilar sequences is very low. Thus, the instant claims are not enabled to the full extent of their scope.

14. Claim 18 is rejected under 35 U.S.C. § 112, first paragraph, enablement, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The instant claim is drawn to methods of detecting a mutated gene using antibodies that recognize the mutated protein gene product; such antibodies must be specific for the mutant protein in the presence of the normal protein to be effective. To produce such antibodies would require undue experimentation.

The factors to be considered in determining whether undue experimentation is required are summarized above. While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

The instant application provides no guidance or working examples in the production of antibodies. More particularly, no guidance is offered for the production of antibodies specific for a mutant BLM protein. The state of the prior art is such that mutant-specific antibodies are rare. While the relative skill of those in the art of making antibodies is high, the art of making antibodies specific to mutant proteins in the presence of the native form of the protein is very little. Additionally, the ability to produce such an antibody is wholly unpredictable. Therefore, Claim 18 is not enabled.

Conclusion

15. Claims 11-20 are not allowed for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (703) 305-1229. The examiner can normally be reached on Monday through Friday, from 8:30am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

KMK
April 18, 2003